CLAIMS

What is claimed is:

1. A pH dependent ion exchange matrix, comprising:

a solid support, and

a plurality of first ion exchange ligands, each first ion exchange ligand comprising:

a cap comprising an amine with a pK of less than about 9;

a spacer covalently attached to the cap, the spacer comprising a spacer alkyl chain with an amine terminus and an acidic moiety covalently attached to the spacer alkyl chain; and

a linker comprising a linker alkyl chain covalently attached to the solid support at a first end of the linker alkyl chain and covalently attached to the amine terminus of the spacer at a second end of the linker alkyl chain;

wherein the matrix has a capacity to adsorb to a target nucleic acid at a first pH, and to release the target nucleic acid at a desorption pH which is higher than the first pH.

2. The matrix of claim 1, wherein the solid support is a silica based material.

3. The matrix of claim 2, wherein the silica based material is a glass fiber.

4. The matrix of claim 2, wherein the silica based material is a silica gel particle.

5. The matrix of claim 4, wherein the silica gel particle is paramagnetic.

6. The matrix of claim 4, wherein the silica gel particle is porous.

7. The matrix of claim 4, wherein the silica gel particle is non-porous.

8. The matrix of claim 1, wherein the cap further comprises an aromatic hydrocarbon ring.

9. The matrix of claim 8, wherein at least one member of the aromatic hydrocarbon ring is the amine with a pK of less than about 9.

10. The matrix of claim 9, wherein the aromatic hydrocarbon ring is selected from the group consisting of pyridine, and imidazole.

11. The matrix of claim 1, wherein the amine with a pK of less than 9 has a pK of at least about 4 and up to about 6.

12. The matrix of claim 1, wherein the acidic moiety is selected from the group consisting of hydroxyl, carboxyl, and carbonyl.

13. The matrix of claim 1, wherein the spacer alkyl chain comprises two (2) to five (5) carbon atoms.

14. The matrix of claim 1, wherein the spacer is selected from the group consisting of cysteine and alanine.

15. The matrix of claim 1, wherein the aromatic hydrocarbon covalently linked to the spacer define a basic amino acid moiety selected from the group consisting of histidine and histamine.

16. The matrix of claim 1, wherein the linker alkyl chain comprises three (3) to eight (8) carbon atoms.

17. The matrix of claim 1, wherein the linker alkyl chain includes at least one member selected from the group consisting of oxygen and amine.

18. The matrix of claim 1, wherein the linker is selected from the group consisting of: glycidine and urea.

19. The matrix of claim 1, wherein the matrix is an anion exchanger capable of exchanging with the target nucleic acid at the first pH, and the matrix has a net neutral or negative charge at the desorption pH.

20. The matrix of claim 1, wherein the desorption pH is at least about 4.0 and up to about pH 10.0.

21. The matrix of claim 1, wherein the matrix can be reused through at least two cycles of adsorption of the target nucleic acid to the matrix at the first pH and of release from the matrix at the desorption pH.

22. A pH dependent ion exchange matrix for isolating a target nucleic acid, comprising:

a silica magnetic particle; and

a plurality of first ion exchange ligands, each first ion exchange ligand comprising:

an aromatic hydrocarbon ring, wherein at least one member of the ring is an amine with a pK of less than about 9;

a spacer covalently attached to the aromatic hydrocarbon ring, the spacer comprising a spacer alkyl chain of with an amine terminus, and an acidic moiety covalently attached to the spacer alkyl chain; and

a linker comprising a linker alkyl chain covalently attached to the silica magnetic particle through a silica residue at a first end of the linker alkyl chain and covalently attached to the amine terminus of the spacer at a second end of the linker alkyl chain;

wherein the matrix has a capacity to adsorb to a target nucleic acid at a first pH, and to release the target nucleic acid at a desorption pH which is higher than the first pH.

23. The matrix of claim 22, wherein the cap further comprises an aromatic hydrocarbon ring.

24. The matrix of claim 23, wherein at least one member of the aromatic hydrocarbon ring is the amine with a pK of less than about 9.

25. The matrix of claim 24, wherein the aromatic hydrocarbon ring is selected from the group consisting of pyridine, and imidazole.

26. The matrix of claim 22, wherein the amine with a pK of less than 9 has a pK of at least about 4 and up to about 6.

27. The matrix of claim 22, wherein the acidic moiety is selected from the group consisting of hydroxyl, carboxyl, and carbonyl.

28. The matrix of claim 22, wherein the spacer alkyl chain comprises two (2) to five (5) carbon atoms.

29. The matrix of claim 22, wherein the spacer is selected from the group consisting of cysteine and alanine.

30. The matrix of claim 22, wherein the aromatic hydrocarbon covalently linked to the spacer define a basic amino acid moiety selected from the group consisting of histidine and histamine.

31. The matrix of claim 22, wherein the linker alkyl chain comprises three (3) to eight (8) carbon atoms.

32. The matrix of claim 22, wherein the linker alkyl chain includes at least one member selected from the group consisting of oxygen and amine.

33. The matrix of claim 22, wherein the linker is selected from the group consisting of: glycidine and urea.

34. The matrix of claim 22, wherein the matrix is an anion exchanger capable of exchanging with the target nucleic acid at the first pH, and the matrix was a net neutral or negative charge at the desorption pH is not.

35. The matrix of claim 22, wherein the matrix can be reused through at least two cycles of adherence of the target nucleic acid to the matrix at the first pH and release from the matrix at the desorption pH.

36. A multimodal pH dependent ion exchange matrix, comprising:

a solid support;

a plurality of first ion exchange ligands, each first ion exchange ligand comprising:

a cap comprising an amine with a pK of less than about 9;

a spacer covalently attached to the cap, the spacer comprising a spacer alkyl chain with an amine terminus; and

a linker comprising a linker alkyl chain covalently attached to the solid support at a first end of the linker alkyl chain and covalently attached to the amine terminus of the spacer at a second end of the linker alkyl chain;

a plurality of second ion exchange ligands, each second ion exchange ligand comprising:

a second alkyl chain; and

a second acidic moiety covalently attached to the second alkyl chain,

wherein the matrix has a capacity to adsorb to a target nucleic acid at a first pH, and to release the target nucleic acid at a desorption pH which is higher than the first pH.

37. The matrix of claim 36, wherein the solid support is a silica based material.

38. The matrix of claim 37, wherein the silica based material is a silica magnetic particle.

39. The matrix of claim 36, wherein the solid support is porous.

40. The matrix of claim 36, wherein the solid support is non-porous.

41. The matrix of claim 36, wherein the cap further comprises an aromatic hydrocarbon ring.

42. The matrix of claim 41, wherein at least one member of the aromatic hydrocarbon ring is the amine with a pK of less than about 9.

43. The matrix of claim 41, wherein the aromatic hydrocarbon ring is selected from the group consisting of pyridine and aniline.

44. The matrix of claim 36, wherein the second acidic moiety is a carboxylic acid residue.

45. The matrix of claim 36, wherein the spacer alkyl chain comprises two (2) to five (5) carbon atoms.

46. The matrix of claim 41, wherein the aromatic hydrocarbon covalently linked to the spacer define a basic amino acid moiety selected from the group consisting of histidine and histamine.

47. The matrix of claim 36, wherein the linker alkyl chain comprises three (3) to eight (8) carbon atoms.

48. The matrix of claim 36, wherein the linker alkyl chain includes at least one member selected from the group consisting of oxygen and amine.

49. The matrix of claim 30, wherein the linker is urea.

50. The matrix of claim 30, wherein the matrix is an anion exchanger capable of exchanging with the target nucleic acid at the first pH, neutral at a second pH which is higher than the first pH, and a cation exchanger at a third pH which is higher than the second pH.

51. The matrix of claim 44, wherein the second pH is at least about 4.0 and up to about pH 10.0.

52. The matrix of claim 30, wherein the proportion of the plurality of first ion exchange ligands and the plurality of second ion exchange ligands covalently attached to the solid phase is designed to ensure that when the matrix comes into contact with a solution

comprising a target nucleic acid at the first pH, the matrix preferentially binds to the target nucleic acid.

53. The matrix of claim 30, wherein the matrix can be reused through at least two cycles of adherence of the target nucleic acid to the matrix at the first pH and release from the matrix at the desorption pH.

54. A method of isolating a target nucleic acid using a pH dependent ion exchange matrix, comprising the steps of:

(a) providing a pH dependent ion exchange matrix comprising:

a solid support, and

a plurality of first ion exchange ligands, each first ion exchange ligand comprising:

a cap comprising an amine with a pK of less than 9, wherein the amine is selected from the group consisting of a primary, a secondary, and a tertiary amine;

a spacer covalently attached to the cap, the spacer comprising a spacer alkyl chain with an amine terminus, and an acidic moiety covalently attached to the spacer alkyl chain; and

a linker comprising a linker alkyl chain covalently attached to the solid support at a first end of the linker alkyl chain and covalently attached to the amine terminus of the spacer at a second end of the linker alkyl chain;

wherein the matrix has a capacity to adsorb to a target nucleic acid at a first pH, and to release the target nucleic acid at a desorption pH which is higher than the first pH.

(b) provide a mixture comprising the target nucleic acid;

(c) combine the mixture and the matrix and incubate at the first pH until the nucleic acid adsorbs to the matrix, forming a complex;

(d) separate the complex from the mixture; and

(e) combine the complex with an elution solution at the desorption pH.

55. The method of claim 54, wherein the solid phase of the matrix provided in step (a) is a silica based material.

56. The method of claim 54, wherein the silica based material is glass fiber.

57. The method of claim 55, wherein the silica based material is a silica gel particle.

58. The method of claim 55, wherein the silica based material is a silica magnetic particle.

59. The method of claim 54, wherein the cap further comprises an aromatic hydrocarbon ring.

60. The method of claim 59, wherein the amine with a pK of less than about 9 is a member of the aromatic hydrocarbon ring.

61. The method of claim 54, wherein the spacer alkyl chain of the matrix provided in step (a) comprises two (2) to five (5) carbon atoms.

62. The method of claim 54, wherein the spacer of the matrix provided in step (a) is selected from the group consisting of cysteine and alanine.

63. The method of claim 54, wherein the aromatic hydrocarbon covalently linked to the spacer of the matrix provided in step (a) define a basic amino acid moiety selected from the group consisting of histidine and histamine.

64. The method of claim 54, wherein the linker alkyl chain of the matrix provided in step (a) comprises three (3) to eight (8) carbon atoms.

65. The method of claim 54, wherein the linker alkyl chain of the matrix provided in step (a) includes at least one member selected from the group consisting of oxygen, amine, and sulphur.

66. The method of claim 54, wherein the linker of the matrix provided in step (a) is selected from the group consisting of: glycidine and urea.

67. The method of claim 54, wherein the matrix provided in step (a) further comprises a plurality of second ion exchange ligands covalently attached to the solid phase.

68. The matrix of claim 54, wherein at least one of the plurality of second ion exchange ligands is a propionate residue.

69. The method of claim 54, wherein the mixture comprising the target nucleic acid material is obtained by disrupting biological material containing the target nucleic acid.

70. The method of claim 54, wherein the target nucleic acid material is RNA.

71. The method of claim 54, wherein the target nucleic acid is DNA.

72. The method of claim 54, wherein the pluralilty of ligands of the matrix provided in step (a) is selected from the group consisting of: histamine via epoxide, histamine via epoxide, histidine via urea, histidine via sulfhydryl, pyridyl alanine, pyridyl cysteine.

73. The method of claim 71, wherein the target nucleic acid is plasmid DNA.

74. The method of claim 71, wherein the target nucleic acid is genomic DNA.

75. A method of making a pH dependent ion exchange matrix, comprising the steps of:

(a) providing a solid phase;

(b) providing a linker comprising an alkyl chain having a first end and a second end; (c) combining the silica based solid phase and the linker under conditions where a covalent bond is formed between the solid phase and the first end of the linker alkyl chain, thereby producing a linker-modified solid phase;

(d) providing an acidic aromatic amine comprising: an aromatic hydrocarbon ring, wherein at least one member of the ring is an amine; a spacer which is covalently attached to the aromatic hydrocarbon, wherein the spacer comprises a spacer alkyl chain with an amino terminus; and an acidic substituent which is covalently attached to the spacer alkyl chain; and

(e) combining the linker-modified solid phase with the acidic aromatic amine under conditions where a covalent bond is formed between the amino terminus of the spacer alkyl chain of the acidic aromatic amine and the second end of the linker.

76. The method of claim 75, wherein the solid phase provided in step (a) is a silica based material.

77. The method of claim 76, wherein the linker is covalently attached to the solid phase in step (c) through a silica residue, wherein the silica residue is covalently attached to a first subunit and a second subunit, wherein the first subunit is selected from the group consisting of: -OH, $-OCH_3$, $-OCH_2CH_3$, and the second subunit is defined by the formula $-(OSiR^1_2)_x-R^1$, wherein R^1 is the same group as the first subunit, and x is at least 0.

78. The method of claim 76, wherein the silica based material is glass fiber.

79. The method of claim 76, wherein the silica based material is a silica gel particle.

80. The method of claim 79, wherein the silica gel particle is paramagnetic.

81. The method of claim 79, wherein the silica gel particle is porous.

82. The method of claim 79, wherein the silica gel particle is non-porous.

83. The method of claim 75, wherein the spacer is selected from a group consisting of cysteine and alanine.

84. The method of claim 75, wherein the aromatic hydrocarbon ring has at least five members.

85. The method of claim 75, wherein the acidic aromatic amine is an amino acid selected from the group consisting of histamine and histidine.

86. A method of making a pH dependent ion exchange matrix, comprising the steps of:

(a) providing a solid support;

(b) providing a first ion exchange ligand comprising:

a cap comprising an amine with a pK of less than 9, wherein the amine is selected from the group consisting of a primary, a secondary, or a tertiary amine;

a spacer covalently attached to the cap, the spacer comprising a spacer alkyl chain and with an amine terminus, an acidic substituent which is covalently attached to the spacer alkyl chain; and

a linker comprising a linker alkyl chain having a first end and a second end, wherein the second end is covalently attached to the amine terminus of the spacer;

(c) combining the solid phase and the first ion exchange ligand under conditions where a covalent bond is formed between solid phase and the first end of the linker alkyl chain.

87. The method of claim 86, wherein the first ion exchange ligand is an imidazole silylurea.

88. The method of claim 87, wherein the acidic substituent of the first ion exchange ligand is a carboxyl residue protected by a methyl group, wherein the methyl group is removed from the carboxyl residue after step (c).

89. The method of claim 86, wherein the method further comprises a step of covalently attaching a second ion exchange ligand precurser to the solid support, wherein the second ion exchange precurser includes an ion exchange terminus blocked by a protecting group.

90. The matrix of claim 89, wherein the method further comprises a step of removing the protecting group from the second ion exchange precurser, forming a second ion exchange ligand.

91. The method of claim 90, wherein the second ion exchange ligand is a cation exchanger at an acidic pH.

92. The method of claim 90, wherein the second ion exchange ligand is negatively charged at an acidic pH.

93. The method of claim 90, wherein relative proportions of a plurality of the first ion exchange residue and a plurality of the second ion exchange residue covalently attached to the solid phase are designed to control the charge ratio on the solid support surface, thereby controlling the binding affinity (capacity remains more a property of the available particle surface) of the solid support to bind to the target nucleic acid material.

94. The method of claim 86, wherein the solid support material is a silica gel particle.

95. The method of claim 94, wherein the silica gel particle is paramagnetic.

96. The method of claim 86, wherein the spacer is selected from a group consisting of cysteine and alanine.

97. The method of claim 86, wherein the cap further comprises an aromatic hydrocarbon ring having at least five members.

98. The method of claim 86, wherein the acidic cap and spacer comprise an amino acid selected from the group consisting of histamine and histidine.

99. A method of making a bimodal pH dependent ion exchange matrix, comprising the steps of:

(a) providing a solid support;

(b) providing a first ion exchange ligand comprising:

a cap comprising an amine with a pK of less than about 9, wherein the amine is selected from the group consisting of a primary, a secondary, or a teritary amine;

a spacer covalently attached to the cap, the spacer comprising a spacer alkyl chain and with an amine terminus; and

a linker comprising a linker alkyl chain having a first end and a second end, wherein the second end is covalently attached to the amine terminus of the spacer;

(c) combining the solid phase and the first ion exchange ligand under conditions where a covalent bond is formed between solid phase and the first end of the linker alkyl chain;

(d) providing a second ion exchange ligand, comprising a second alkyl chain and an acidic residue covalently attached thereto, wherein the acidic residue has a protective group covalently attached thereto;

(e) combining the solid phase with the first ion exchange ligand attached thereto with a second ligand under conditions which promote formation of a covalent bond between the protected second ion exchange ligand and the solid phase; and

(f) deprotecting the acidic residue of the second anion exchange ligand by removing the protective group therefrom.

100. The method of claim 99, wherein the second ion exchange ligand is a propionate residue.